REMARKS

Claims 35-63 are pending in this application. Claims 43-53 and 58-63 are withdrawn from consideration in a response to a restriction requirement made on April 7, 2002. Claims 35-42 and 54-57 are rejected. Claim 42 is objected to. Claims 35-42 and 54-57 were examined on the merits. Claims 38-42 and 54 are cancelled. Claims 35-37 and 55 are amended herein. Support for amended claims 35-37 and 55 can be found at page 6, line 23 through page 7, line 24 of the specification as well as throughout the examples and the claims as originally filed. Thus, no new matter is added.

Specification

The specification is objected to at pages 35, 37 and 43 because it contains embedded hyperlinks. Applicants herein amend pages 35, 37 and 43 of the specification, removing the hyperlinks.

Claims Objection

Claim 42 is objected to for an informality. Applicants herein cancel claim 42, thus, rendering the objection to this claim moot.

35 U.S.C. § 112, second paragraph

Claims 35, 36, 38-42 and 54-57 stand rejected under 35 U.S.C. § 112, second paragraph for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. In particular, the Examiner alleges that the metes and bounds of claims 35 and 36 are unclear in that they,

"appear to say that the claimed genus structure is compared with an alignment of SEQ ID NO:2 with some other sequence." Applicants herein amend claim 35 to recite:

> An immunogenic composition comprising a fusion protein comprising an amino acid sequence which has at least 90% identity to SEQ ID NO:2 over the entire length of SEQ ID NO:2 and a fusion partner; wherein the immunogenic composition, when administered to a subject, induces an immune response that recognizes a polypeptide having the sequence of SEQ ID NO:2.

Therefore, Applicants respectfully submit that claim 35 no longer recites fragments of SEQ ID NO:2 that are aligned with SEQ ID NO:2. Thus, the rejection of claims 35 and 36 is rendered moot.

The Examiner notes that the phrase, "the aligned sequence" in clams 39 lacks antecedent basis. Applicants herein cancel claim 39, thus, rendering rejection of this claim moot.

Applicants respectfully submit that in view of the forgoing remarks and the claims as amended, Applicants have overcome the Examiner's rejections under 35 U.S.C. §112, second paragraph, and that the rejection of claims 35, 36 and 55-57 should be withdrawn. Applicants herein cancel claims 38-42 and 54, thus rendering the rejection of these claim moot.

35 U.S.C. § 112, first paragraph

Claims 35, 36, 38-42, and 54-57 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Relying on *University of California v. Eli Lilly and Company*, 119 F.3d. 1559 (Fed. Cir. 1997), the Written Description Guidelines issued by the USPTO, *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d. 1316 (Fed Cir. 2002), and *Vas-Cath Inc. v. Mahurkar*, 19

U.S.P.Q.2d 1111 (Fed. Cir. 1991), the Examiner alleges that claims 35 and 36 do not recite a function coupled to the structure of the claimed genus. The Examiner alleges that, "an immune response does not appear to be the function coupled to the structure of the claimed genus" because Ezzell (*J. NIH Res*, 1995 7:46-49) teach that MAGE-1 and other structurally unrelated proteins to the instant SEQ ID NO:2 induce cell-mediated response. The Examiner also suggests that Van den Eynde, *et al.* (*J. Exp. Med* 1999 Vol. 190, pages 1793-1799) teach that the protein sequence shown in Figure 3 and many other proteins, such as TRP1 and NY-ESO-1, that are structurally unrelated to SEQ ID NO:2 also induce an immune response. The Examiner then alleges that activated T-cells or antibodies would be of a different genus than the polypeptides recited in the claims.

Applicants traverse these rejections, and they respectfully submit that the Examiner's reliance on Ezzell and Van den Eynde, *et al.* is unclear. However, Applicants believe that the Examiner is incorrectly relating any function associated with T-cells or antibodies generated by the polypeptides recited in the claims as the same function associated with the polypeptides recited in the claims. Applicants respectfully submit that claims 35-42 and 54-57 are directed to immunogenic compositions comprising polypeptides that induce an immune response to SEQ ID NO:2. The recited function is a function of the recited polypeptides, not the T-cells or antibodies that may be induced by them.

The Examiner also alleges that claims 35 and 36 lack written description because there is, "substantial variability among the species of polypeptides." The Examiner further alleges that these polypeptides are structurally unrelated. Applicants traverse these rejections. Applicants disclose within the specification the entire sequence of SEQ ID NO: 2. Applicants also disclose, at several places within the specification, definitions

of variants and homologs as well as an algorithm for determining sequence identity. See, for instance, page 27, line 16 through page 31, line 2 of the specification. In addition, Applicants disclose peptide fragments incorporating epitopes of CASB618. See, for instance, page 3, lines 3-5 of the specification. However, in an effort to further prosecution, Applicants herein amend claim 35 to recite a fusion protein comprising an amino acid having at least 90% sequence identity to SEQ ID NO:2 over the entire sequence of SEQ ID NO:2 and a fusion partner. Support for this amendment can be found at page 6, line 23 through page 7, line 24. Applicants respectfully submit that, as amended, claim 35 recites structurally related polypeptides that find support within the specification. Accordingly, Applicants request that the rejection of this claim and all dependent claims be removed.

Claim 42 also stands rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking written description. Applicants cancel claim 42 herein, thus rendering the rejection of this claim moot.

Claims 38, 39-41 and 54-57 also stand rejected as dependent claims of rejected base, "claim 1." Applicants respectfully submit that the Examiner appears to mean, "base claim 35" not, "claim 1" and have responded accordingly. Specifically, the Examiner relies on *Vas-Cath v. Mahurkar,* 19 U.S.P.Q.2d. 1111 (Fed. Cir. 1991) and alleges that the specification does not, "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." The Examiner further alleges that the specification has only disclosed SEQ ID NO:2 and the skilled artisan, "cannot envision the detailed chemical structure of the genus of proteins." Applicants traverse these rejections. As discussed above, the specification is replete with example of epitopes of SEQ ID NO:2 having at least 90% sequence identity to an aligned contiguous segment of

SEQ ID NO:2 that has at least 90% sequence identity to SEQ ID NO:2. In addition, Applicants provide, in Example 7 of the specification, several examples of peptide fragments of SEQ ID NO:2 for stimulating immunoresponse. However, as noted above, in order to advance prosecution Applicants herein amend claim 35 to recite a fusion protein comprising an amino acid having at least 90% sequence identity to SEQ ID NO:2 over the entire sequence of SEQ ID NO:2 and a fusion partner. Applicants respectfully submit that based upon the written description provided within the specification the skilled artisan could recognize that Applicants invented what is claimed in amended claim 35, as well as in dependent claims 55-57. Applicants herein cancel claims 38-41 and 54, thus rendering the rejection of these claims moot.

Claims 35-42 and 54-57 also stand rejected under 35 U.S.C. § 112, first paragraph for allegedly not "reasonably providing enablement for inducing immune response in a human subject." Specifically, the Examiner alleges that the specification does not establish whether SEQ ID NO:2 is a cancer antigen. The Examiner also alleges that up-regulation of mRNA of a polypeptide does not necessarily indicate that a polypeptide is over-expressed in a mammalian cell line. Furthermore, the Examiner alleges that even if SEQ ID NO:2 is determined to be a colon cancer antigen, "inducing an immune response against a cancer antigen that is also expressed in normal cells is not a trivial matter."

Applicants traverse these rejections. Applicants respectfully submit that mRNA levels in tissue are typically used by the skilled artisan to determine protein expression levels. The Examiner alleges the mRNA transcription does not always correspond with translation. In arguing this point the Examiner relies on very specific examples to make a general conclusion of the correlation regarding mRNA transcription and translation. The Examiner cites Alberts, *et al.* (*Molecular Biology of the Cell*, 3rd edition, 1994, page 465)

as teaching that translation of ferritin mRNA into polypeptide is blocked during periods of iron starvation. The Examiner also cites Shantz and Pegg (*Int J of Biochem and Cell Biol.* 1999 Vol. 31 pp. 107-122) as teaching that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of mRNA; McCLean and Hill (*Eur J of Cancer*, 1993, vol. 29A pp. 2243-2248) as teaching p-glycoprotein can be over-expressed in cells without over expression of mRNA; and Fu, *et al.* (*EMBO Journal*, 1996, Vol. 15, pp 4392-4401) as teaching that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patient without mutation in the p53 gene.

Applicants respectfully submit that all of these examples, cited by the Examiner, relate to specific polypeptides in which translation may be effected by cofactors, secondary structure and/or genetic mutation. Thus, Applicants respectfully submit that Examiner appears to rely on very specific examples to refute the accepted correlation made by the skilled artisan of mRNA levels with protein expression. Furthermore, Applicants respectfully submit that following reference with a form 1449 as exemplifying that mRNA production correlates with protein production in many instances. See Gimmi, *et al. Nucleic Acids Res.* 16(18):8977-8997 (1998). Applicants, therefore, submit that by providing an analysis of mRNA expression from various tissue samples, they provide enablement to the skilled artisan in understanding that CASB618 is over-expressed in colon cancer cells. Furthermore, Applicants respectfully submit that because Applicants demonstrate that CASB618 is over-expressed in cancer colon cells compared with normal colon cells, it can be considered a cancer antigen. Thus, Applicants respectfully traverse the Examiner's allegation that Applicants have not determined whether CASB618 is a cancer antigen.

The Examiner also alleges that, "even if SEQ ID NO:2 is determined to be a colon cancer antigen, inducing an immune response against a cancer antigen that is also expressed in normal cells is not a trivial matter in the state of the art." Specifically, the Examiner cites Riott, *et al.* (*Immunology*, Fourth Edition, 1996, Mosby, pages 7.8-7.12, and Chapter 10 only), as stating that only a minority of peptide fragments from a protein antigen can bind particular MHC molecules. The Examiner also alleges that U.S. Patent No. 5,840,839 teaches that finding peptides that bind MHC molecules and stimulate immune response is not a trivial matter. Furthermore, the Examiner alleges that Ezzell (*supra*), Spitler (*Cancer Biotherapy*, 1995, 10:1-3), and Boon (*Adv Can Res*, 1992, 58:177-210) teach the lack of predictability in cancer vaccines. Finally, the Examiner cites Benjamini and Leskowitz (*supra*) and alleges that, "animals normally do not response immunologically to self."

Applicants amend claim 35 herein to recite an immunogenic composition comprising a fusion protein comprising an amino acid having 90% sequence identity to SEQ ID NO:2 and a fusion partner. Fusion proteins are described in detail in at page 6, line 23 through page 7, line 24. In addition, the specification describes fusion partners as assisting in providing T-helper epitopes (immunological fusion partners); see for instance, page 7, lines 4-10 of the specification. Applicants submit that claims 35 no longer recites an immunogenic composition comprising SEQ ID NO:2 alone, a variant of SEQ ID NO:2 alone or epitopes from SEQ ID NO:2 alone. Thus, claims 35, as amended, is not directed to a self-protein or epitopes of a self-protein, because the polypeptides of claim 35 also comprise a fusion partner that can assist in T cell recognition of a variant of SEQ ID NO:2. Applicants, therefore, submit that, as amended, claim 35 is in condition for allowance and rejection of this claim under 35 U.S.C. § 112, first paragraph be removed.

Furthermore, as claims 36-37 and 55-57 depend from claims 35, claims 36-37 and 55-57 are also in condition for allowance. Claims 38-42 and 54 are cancelled herein, thus, rendering the rejection of these claims moot.

For the reasons provided above, Applicants traverse this rejection and request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

35 U.S.C. § 101

Claims 35-42 and 54-57 stand rejected under 35 U.S.C. § 101 for allegedly not being supported by a substantial asserted utility or a well established utility. Specifically, the Examiner relies on arguments made in the previous section regarding predictability of protein expression compared with mRNA expression in a cell. The Examiner alleges that there is no correlation between mRNA expression and protein expression. Thus, the Examiner then alleges that Applicants have not established that SEQ ID NO:1 could be a biomarker for colon cancer.

Applicants respectfully traverse these rejections. Applicants show in several places within the specification that CASB618 is over-expressed in colon tumors cells compared with normal colon cells. See for instance Figure 1. Furthermore, Figure 2 demonstrates that CASB618 is not expressed in large amounts in various types of normal tissue other than colon. As Applicants argue above, the Examiner appears to rely on very specific examples to refute the generally applied correlation by the skilled artisan of mRNA levels with protein expression. Furthermore, Applicants respectfully submit that following reference as an example the mRNA production correlates with protein production in many instances. See Gimmi, *et al. (Supra).* Applicants therefore, submit that they demonstrate that CASB618 is over-expressed in colon cancer cells compared

with normal colon cells in the specification. Thus, the over expression of CASB618 is associated with colon tumor cells and provides a possible target for immunotherapy against colon cancer. Therefore, Applicants provide both a substantial and well established utility for the claimed invention.

For the reasons provided above, Applicants traverse this rejection and request that the rejection under 35 U.S.C. § 101 be withdrawn. Applicants herein cancel claims 38-42 and 54, thus rendering rejection of these claims moot.

35 U.S.C. § 102

Claims 35, 36, 38-41 and 54 stand rejected under 35 U.S.C. § 102 as allegedly being anticipated by Mankovich, *et al.* (1989, *Journal of Bacteriology*, vol. 171, pages 5325-31) as evidenced by Benjamini and Laskowski (1991, *Immunology, A Short Course*, Wiley-Liss, Chapter 3, pages 37-45 only). Specifically, the Examiner alleges that Makovich, *et al.* at page 5328 (Figure 2) teach an isolated polypeptide comprising a fragment 100% identical to amino acids 98-105 of SEQ ID NO:2. The Examiner also alleges that Benjamini and Leskowitz evidence that a fusion protein comprising the amino acid fragment of Mankovich, *et al.* would induce an immune response to SEQ ID NO:2. The Examiner further alleges that mutL of Mankovich, *et al.* would act as a heterophile antigen with respect to SEQ ID NO:2.

Applicants amend claim 35 herein to recite an immunogenic composition comprising a fusion protein comprising an amino acid having at least 90% sequence identity to SEQ ID NO:2 over the entire sequence of SEQ ID NO:2 and a fusion partner. Applicants believe that this amendment renders the Examiner's rejection moot. In addition, Applicants herein cancel claims 38-41 and 54, thus rendering rejection of these claims moot.

In view of the foregoing remarks, the Applicants respectfully request that the Examiner withdraw this rejection based on 35 U.S.C. §102(b) of claims 35 and 36.

35 U.S.C. § 103

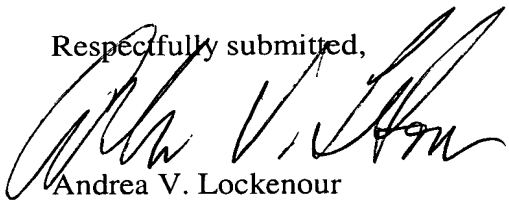
Claims 55-57 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Mankovich, *et al.* (1989, *Journal of Bacteriology*, vol. 171, pages 5325-31) in view of WO 95/17210 (29 June 1995). Specifically, the Examiner alleges that Mankovich, *et al.* teach an epitope of SEQ ID NO:2 while WO 96/17210 teach TH1-inducing adjuvants.

As discussed above, Applicants amend claim 35 herein to recite an immunogenic composition comprising a fusion protein comprising an amino acid having at least 90% sequence identity to SEQ ID NO:2 over the entire sequence of SEQ ID NO:2 and a fusion partner. As claims 55-57 depend from amended claim 35, Applicants believe that this amendment renders the Examiner's rejection moot.

In view of the foregoing remarks, the Applicants respectfully request that the Examiner withdraw these rejections of claims 55-57 under 35 U.S.C. §103(a).

Applicants reserve the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the cancelled claims, the claims as originally filed, and any other claims supported by the specification. Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited. If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicants' undersigned attorney.

Respectfully submitted,



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